

REMARKS

Present Status of the Application

Claims 9-16 were rejected under 35 U.S.C. 112, second paragraph as being indefinite. Claims 9-16 were rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirements or as based on a disclosure which is not enabling. The Office Action further mentioned that the attempt to incorporate subject matters by reference to GenBank accession numbers and NCBI SNP database is ineffective.

Claims 9-12 have been amended to recite active process steps for clarification. A new Sequence Listing incorporating related sequences of the Gene Bank Accession Number NM-022162 (as SEQ ID No. 13) and NG_007508.1 (as SEQ ID NO. 14) has been provided for clarification purposes. The specification has been amended accordingly for clarification and correcting informalities. It is believed that the amendments are supported by the original specification and drawings of this application and can overcome the objections. Entry of the amendments to the specification is respectfully requested.

After entering the amendments and considering the following discussions, a notice of allowance is respectfully solicited.

Regarding the "Incorporation by Reference" issues

Regarding the confusions mentioned in the Office Action dated March 18, 2009, according to the suggestions of the Examiner Weise over the phone with the Patent Agent Huang,

Applicant has submitted a new Sequence Listing in both computer readable form (CRF) and paper copy. The new Sequence Listing incorporates additional sequences of the Gene Bank Accession Number NM-022162 (as SEQ ID No. 13) and NG_007508.1 (as SEQ ID NO. 14), for clarifying the discrepancies and errors regarding the sequences denoted by the GenBank accession numbers from NCBI SNP database of the present application. Applicant confirms that the paper and electronic versions of the newly submitted Sequence Listing are identical.

Discussion of 112 rejections

Claims 9-16 were rejected under 35 U.S.C. 112, second paragraph as being indefinite.

Claims 9-12 have been amended to recite active process steps to overcome the indefinite rejections and for clarification. Entry of such amendments is respectfully requested.

Withdrawal and reconsideration of such 112 rejections are earnestly requested.

Claims 9-16 were rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirements or as based on a disclosure which is not enabling.

The Office Action is of the opinion that discrepancies are found between the gene sequences listed in the specification of the present application and the gene sequences recorded in the NCBI SNP database. In details, in point (A), the sequence with accession No. AC07728 includes more genes than the NOD2 gene and has four different versions. In point (B), the sequence with accession No. AQ534686 is shorter than the full NOD2 gene. In point (C), the sequence with accession No. NM_022162 is listed with different positions of SNP8, 12 and 13.

In point (D), Alignment of the primers reveals that these primers flank positions are identified by the Applicant, rather than the database.

A new Sequence Listing has been provided for clarification purposes, and the specification has been amended accordingly for clarification and correcting informalities, as discussed in the following paragraphs.

Concerning points (A). and (B)

In order to better define clearly the genomic sequence of NOD2/CARD15 gene, with the help available from the NCBI data base, a sequence of Gene Bank Accession Number NG_007508.1 from the NCBI data base is provided.

The genomic sequence (Gene Bank Accession Number NG_007508.1) comprises the whole sequence of the NOD2/CARD15 gene and only this sequence starting from nucleotide position 5001 to position 40938.

In fact, according to the description of the present application, it is possible for one skilled in the art to identify the sequence part which describes the NOD2/CARD15 gene, when considering the Accession Number AC007728 (chromosome 16) together with the information concerning the position of the NOD2/CARD15 gene on chromosome 16 at page 2, lines 17 – 19 of the specification. That is, on the basis of the sequence of chromosome 16 and locus information for NOD2/CARD15 gene, a person skilled in the art can easily identify the sequence part which describes the NOD2/CARD15 gene.

In this case, Gene Bank Accession Number NG_007508.1 from the NCBI data base is incorporated to the specification and a new Sequence Listing including additional sequences of

the Gene Bank Accession Number NM-022162 (as SEQ ID No. 13) and NG_007508.1 (as SEQ ID NO. 14) is provided for easy references and clarification. The Gene Bank Accession number AQ534686 has been deleted from the specification.

Accordingly, the third and fourth paragraphs of page 2 of the specification have been amended.

Concerning point C.

The sequence NM-022162 is an mRNA sequence which offers two possibilities to number the nucleotides of the sequence. Both possibilities are presented in the NCBI database. First possibility is to number the sequence starting with number 1 at the first nucleotide. Second possibility is to start numbering at the nucleotide A which belongs to the codon for translation start. The first nucleotide of the sequence and nucleotide A of the start codon are 105 nucleotides apart. Thus, the positions of SNPs given in the present application and the positions found by the Office Action (the Examiner) correspond as shown in the following table.

SNP	Position in NM_022162.1 (translation start=+1) Examiner	Position in NM_022162.1 (first nucleotide =+1) present application	NCBI RefSNP old denomination	NCBI RefSNP new denomination
8	c.2104C>T	2209C>T	ss2978536	rs2066844
12	c.2722G>C	2827G>C	ss2978537	rs2066845
13	c.3016_3017insC	3121insC	ss2978539	rs2066847
13	c.3019_3020insC	3124insC		rs5743293

Concerning SNP 13 the NCBI data base contains an error. There are two different positions presented. According to literature only SNP 13 with position c.3019 / 3124 / rs5743293 is valid.

Thus, positions of SNPs as presented in the present application are correct.

By searching the NCBI databases in order to explain the discrepancies mentioned by the Examiner, it is discovered that the wrong denomination for SNP 13 at position c.3019 / 3124 (see page 3, paragraph 3, lines 13-18 of the description) may be used. As this is an obvious error we would like to correct it in the description. Thus, denomination ss2978539 should be amended to read rs5743293.

Accordingly, the last third paragraph of page 3 of the specification has been amended.

In general, the doubled numbering system and the error of the database may bring about misunderstandings, as mentioned by the Office Action. Thus, it is better to introduce the genomic sequence of NOD2/CARD15 gene according to Accession Number NG_007508.1. Within this sequence the position of the SNPs can be uniquely defined as shown in the next table.

SNP	Position in NM_022162.1 (translation start=+1) Examiner	Position in NM_022162.1 (first nucleotide =+1) present application	NCBI RefSNP new denomination	Position in genomic DNA NG_007508.1
8	c.2104C>T	2209C>T	rs2066844	g.19877C>T
12	c.2722G>C	2827G>C	rs2066845	g.30491G>C
13	c.3019_3020insC	3124insC	rs5743293	g.37732_37733 insC

Concerning point D.

According to the Office Action, the primers of the present application flank the positions of SNPs given in the present application but not the positions found by the Examiner. This is due to the fact that the alignment program uses the numbering starting at the first nucleotide in sequence

NM-022162. If the alignment program used the numbering starting at nucleotide A of the start codon of sequence NM-022162, the primers would flank the positions of the SNPs found by the Examiner.

Thus, also the primers possess the correct sequence to hybridize to positions flanking the SNPs and are therefore suitable to fulfill their expected function to identify SNPs 8, 12 or 13 in the NOD2/CARD15 gene if present.

The sequence NG_007508.1 marked with the positions of the SNPs, of the probes and of the primers is provided for references (Appendix I).

As discussed above, upon the entry of the above amendments, the disclosure of the present application should meet the written description requirement and enablement requirement for the claimed subject matters of amended claims.

Accordingly, withdrawal and reconsideration of these 112 rejections are respectfully requested.

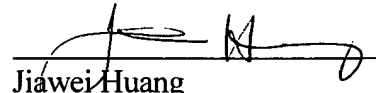
CONCLUSION

For at least the foregoing reasons, it is believed that the pending claims 9-16 of the present application patently defines over the prior art and are in proper condition for allowance. If the Examiner believes that a telephone conference would expedite the examination of the above-identified patent application, the Examiner is invited to call the undersigned.

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